# RESPONSE

## II. IDS issues

Applicants include as **Exhibit A** the information available regarding the chromosome 19 clone that describes Reference CP on the Form PTO-1449, filed November 21, 2002. This information describes all of the dates associated with this submission.

The Examiner is correct that the International Search Report is included and would be reference CQ, it was not labeled because it was not intended citation. All of the relevant art cited in the International Search Report appears on the Form PTO-1449, individually. Applicants included the International Search Report on the Form PTO-1449 in the interests of full disclosure, as it demonstrates the time at which Applicants became aware of such information.

## II. Status of the Claims

This Response contains no changes to the pending claims. Claims 1-3, and 5 are therefore presently pending in the case.

## III. Rejection of Claims Under 35 U.S.C. § 101

Claims 1-3 and new claim 5 are rejected under 35 U.S.C. § 101 for the reasons already of record on pages 3-5 of the Office Action dated 12/17/02.

Applicants respectfully disagree and will limit most of their rebuttal to the evidence of utility, rather than argue the applicability of cited case law, but reserve the right to do so should it become necessary at a latter time. Applicant's representative would like to note for the record that the references to the present invention as a G protein-coupled receptor (made in their previous response) were the unintentional result of a clerical error and that Applicant's Representative are aware of no such association.

Applicants begin by noting that the Action (on page 4, lines 25-26) objects to Applicants use of this post filing information on the basis that allegedly they do not support assertions made in the specification. However this is incorrect, as in the specification Applicants have asserted that the present

invention encodes an ion channel protein (see, at least, the title, specification Section 2 and page 3, second paragraph). Ion channel proteins are well known to those of skill in the art, this is particularly true for voltage-gated potassium channels and the sequences of the present invention encode a voltage-gated potassium channel, KCNA7. The specification details tissues in which these sequences are expressed (heart and others at page 3, lines 31-34) and disease associations(particularly the cardiac related disorders high blood pressure, arrhythmia, and others at page 13, lines 22-24) both of which are consistent with the evidence provided in information provided by others in a scientific publications (Bardien-Kruger, S., *et al.*, Eur J Hum Genet, 10(1):36-43, 2002 and Kashuba *et al.*, Gene, 268(1-2):*115-22*, 2001 (CO on Form -1449). In addition to the sequence identity information provided in the previous response, Applicants have also provided clear evidence that the sequences of the present invention map to what is now recognized as the gene encoding the voltage-gated potassium channel, KCNA7. Thus Applicants have provided evidence that the sequences of the present invention which were asserted in the specification to encode a novel human ion channel protein do indeed encode the voltage-gated potassium channel, KCNA7. This evidence includes sequence identity, tissue expression, disease association and genetic mapping to the same loci. Thus clearly Applicants assertions that the present invention encode a human ion channel protein, particularly the voltage-gated potassium channel KCNA7, are well supported.

In Applicant's previous response, evidence of the credibility of Applicant's assertion that the sequences of the present invention encode an ion channel, Applicants have submitted evidence that the sequences of the present invention encode a nucleic acid which has been annotated by third party scientists, wholly unaffiliated with Applicants, as encoding *Homo sapiens* voltage-gated potassium channel KCNA7 mRNA(GenBank accession no. AF315818). Additional evidence was provided in the form of a nucleic acid sequence comparison between SEQ ID NO:1 and AF315818 wherein a high degree of homology (99.927 % identity) over the vast majority of the sequence was presented.

Currently applicants respectfully submit further evidence that the sequences of the present invention in fact encode *Homo sapiens* voltage-gated potassium channel KCNA7 (GenBank accession nos. AF315818(nucleotide) and AAK63002(protein)). Applicants submit a amino acid sequence comparison between SEQ ID NO:2 and GenBank accession no. AAK63002 which has been annotated by third party scientists, wholly unaffiliated with Applicants, as encoding *Homo sapiens*

voltage-gated potassium channel KCNA7 (comparison and information provided as **Exhibit B**). At the amino acid level these proteins are 99.781% identical over their full length.

As further evidence of the specific utility of the sequences of the present invention in localizing the specific region of the human chromosome and identification of functionally active intron/exon splice junctions was the in formation provided as Exhibit G of Applicant's previous response. This evidence indicates that the sequence of the present invention is encoded by 2 exons spread non-contiguously along a region of human chromosome (19q13.3), which is represented by clone AC008687.5. Thus clearly one would not simply be able to identify the protein encoding exons that make up the sequence of the present intention, nor to map the protein encoding regions identified specifically by the sequences of the present invention without knowing exactly what those specific sequences were. Additionally, it should be noted that the gene of AF315818, *Homo sapiens* voltage-gated potassium channel KCNA7 mRNA also maps to the same region of human chromosome 19 (essentially position 49.2M on 19q13.3). This evidence clearly provides additional support to Applicant's assertion that the sequences of the present invention encode the human *Homo sapiens* voltage-gated potassium channel, KCNA7. This information and the use of the sequences of the present invention in chromosome mapping and identification of intron/exon boundries, wasdescribed in the specification as filed (at least at page 3, lines 1-5).

These multiple source of information provide clear and convincing evidence that those of skill in the art would recognize the present invention as an ion channel protein, more specifically KCNA7, whose function is described in the scientific publications entitled "Characterization of the human voltage-gated potassium channel gene, KCNA7, a candidate gene for inherited cardiac disorders, and its exclusion as cause of progressive familial heart block I (PFHBI)."(Bardien-Kruger, S., *et al.*, Eur J Hum Genet, 10(1):36-43, 2002, previously submitted). Thus clearly, there can be no question that Applicants' asserted utility for the described sequences is "credible." Applicants have thus supplied evidence supporting their assertion that those of skill in the art would recognize that the sequences of the present invention encode a ion channel protein, more particularly that of voltage-gated potassium channel KCNA7 and has all the recognized uses thereof. In contrast, the Examiner has provided no evidence of record indicating that those of skill in the art would not recognize the sequences of the present invention as encoding an ion channel protein. The Examiner has only provided rare examples in which sequence and structural homology is alleged not to be predictive of function.

Additionally, with regard to the citation of the occasional journal article submitted to support an allegation of a lack of utility, the PTO has repeatedly attempted to deny the utility of nucleic acid

sequences based on a small number of publications that call into doubt prediction of protein function from homology information and the usefulness of bioinformatic predictions, of which these articles are merely the latest examples. Applicants agree that there is not 100% consensus within the scientific community regarding prediction of protein function from homology information, and further agree that prediction of protein function from homology information is not 100% accurate. However, Applicants respectfully point out that the lack of 100% consensus on prediction of protein function from homology information is irrelevant to the question of whether the claimed nucleic acid sequence has a substantial and specific utility, and that 100% accuracy of prediction of protein function from homology information is **not the standard** for patentability under 35 U.S.C. § 101. Applicants respectfully point out that, as discussed above, the legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be **believable**. Applicants submit that the overwhelming majority of those of skill in the relevant art would **believe** prediction of protein function from homology information and the usefulness of bioinformatic predictions to be powerful and useful tools, as evidenced by extensive number of journal articles (which support Applicants' assertion that the overwhelming majority of those of skill in the art place a high value on prediction of protein function from homology information and the usefulness of bioinformatic predictions), and would thus **believe** that Applicants sequence is an ion transporter protein, voltage-gated potassium channel KCNA7, whose function is described. As **believability** is the standard for meeting the utility requirement of 35 U.S.C. § 101, and **not** 100% consensus or 100% accuracy, Applicants submit that the present claims must clearly meet the requirements of 35 U.S.C. § 101. Even the **PTO itself** does not require 100% identity between proteins to establish functional homology. The Examiner's position that homology of SEQ ID No:1 to a known DNA molecule with a known function does not endow SEQ ID NO:1 with the function is contrary to Example 10 of the PTO's Revised Interim Utility Guidelines Training Materials (pages 53-55), which establishes that a rejection under 35 U.S.C. § 101 as allegedly lacking a patentable utility and under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility, is not proper when there is no reason to doubt the asserted utility of a full length sequence (such as the presently claimed sequence) that has a similarity score of 95% to a protein having a known function. In the Analysis portion of Example 10 it states that "Based on applicant's disclosure and the results of the PTO search, there is no reason to doubt the assertion that SEQ ID NO:2 encodes a DNA ligase. Further DNA ligases have a well-

established use in the molecular biology art based on this class of proteins ability to ligate DNA. .....Note that if there is a well-established utility already associated with the claimed invention, the utility need not be asserted in the specification as filed..... Thus the conclusion reached from this analysis is that a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph, utility rejection should not be made."

The present case is the same as that presented in Example 10 of the Revised Interim Utility Guidelines Training Materials (pages 53-55). In the present case it is clear that the sequences of the present invention encode a ion channel proteins (voltage-gated potassium channel KCNA7 which has been characterized). Ion channel proteins, particularly voltage-gated potassium channels, have a well-recognized and well-established utility and value to those of skill in the art, particularly as drug targets in the pharmaceutical industry. Thus a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph, utility rejection should not have been made and should be withdrawn.

In addition to those utilities presented above and in Applicant's previous response, a still further example of utility is the use of the present sequences in such diagnostic assays as those associated with identification of paternity and forensic analysis, among others (for example, the specification at page 8, line 20, page 3,line 19 and page 12, lines 2-4). The sequences of the present invention have particular utility as the application as filed identified several polymorphisms (page 16, line 33 through page 17, line 9). The identified polymorphisms include a G/C transversion in the sequence region corresponding to, for example, nucleotide position number 566 of SEQ ID NO:1 (resulting in a arg or pro being present at corresponding amino acid position 189 of, for example, SEQ ID NO:2); and a T/C transition in the sequence region corresponding to, for example, nucleotide number 1253 of SEQ ID NO:1 resulting in an met or thr being present at corresponding amino acid position 418 of, for example, SEQ ID NO:2).

This is also not a case of a potential utility. Applicants respectfully submit that even in the worst case scenario, the described polymorphisms are each useful to distinguish 50% of the population (in other words, the marker being present in half of the population) and that the ability of a polymorphic marker to distinguish at least 50% of the population is an inherent feature of any polymorphic marker, and this feature is well understood by those of skill in the art. Applicants note that as a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988). Applicants support for Applicants' assertion of utility is provided by the

fact that the skilled artisan would readily recognize and easily believe that the presently described polymorphic markers could be useful in forensic analysis. The fact that forensic biologists use polymorphic markers such as those described by Applicants every day provides more that ample support for the assertion that forensic biologists would also be able to use the specific polymorphic markers described by Applicants in the same fashion. Therefore, again it is clear that the sequences of the present invention have utility.

Given the physiologic activity and importance of ion channel proteins as known to those of skill in the art, those of skill in the art would readily appreciate the importance of tracking the expression of the genes encoding the described proteins, particularly due to the established role of ion channel proteins in human disorders, such as but not limited to, obesity, high blood pressure, connective tissue disorders, infertility, diabetes, alopecia and arrhythmia (specification at page 13, lines 22-24). Applicants respectfully point out that nucleic acid sequences have the greatest specific utility in gene chip applications once the role of the sequence has been identified (ion channel protein) and so have tissues of interest (specification at page 3, lines 31-34), as in the present case. Once the role of the particular nucleic acid is known, the level of gene expression has and even greater significance. By identifying the physiological activity role of the claimed sequence, the claimed sequence has a far greater utility in gene chip applications that just any random piece of DNA. Applicants respectfully submit that **specific** utility, which is the proper standard for utility under 35 U.S.C. § 101, is distinct from the requirement for a **unique** utility, which is clearly an improper standard. As clearly stated by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991; "*Carl Zeiss*"):

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility." *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

Therefore, just because other nucleic acid sequences find utility in gene chip applications does not mean that the use of Applicants' sequence in gene chip applications is not a specific utility. Furthermore, the requirement for a unique utility is clearly not the standard adopted by the Patent and Trademark Office. If every invention were required to have a unique utility, the Patent and Trademark Office would no

longer be issuing patents on batteries, automobile tires, golf balls, golf clubs, and treatments for a variety of human diseases, such as cancer and bacterial or viral infections, just to name a few particular examples, because examples of each of these have already been described and patented. All batteries have the exact same utility - specifically, to provide power. All automobile tires have the exact same utility - specifically, for use on automobiles. All golf balls and golf clubs have the exact same utility - specifically, use in the game of golf. All cancer treatments have the exact same utility - specifically, to treat cancer. All anti-infectious agents have the exact same broader utility - specifically, to treat infections. However, only the briefest perusal of virtually any issue of the Official Gazette provides numerous examples of patents being granted on each of the above compositions every week. Furthermore, if a composition needed to be unique to be patented, the entire class and subclass system would be an effort in futility, as the class and subclass system serves solely to group such common inventions, which would not be required if each invention needed to have a unique utility. Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

Thus in summary, Applicants have described novel nucleic and amino acid sequences, their tissue specific expression, disease associations and naturally occurring polymorphisms that exist within these molecules. Furthermore, the sequences of the present invention encode a human voltage-gated potassium channel (a protein class with well recognized utility) more specifically the human voltage-gated potassium channel KCNA7, a protein whose function is known to those of skill in the art. Thus the present case parallels Example 10 of the PTO's Revised Interim Utility Guidelines Training Materials (pages 53-55) and given the many utilities described for the sequences of the present invention, Applicants respectfully submit that the rejection of the presently claimed invention under a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph utility rejections should be withdrawn.

## IV. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

Claims 1-3 and new claim 5 are also rejected under 35 U.S.C. § 112 first paragraph for the reasons already of record on page 6 of the Office Action dated 12/17/02 as well as for the reasons given in the above rejection under 35 U.S.C. § 101.

Applicants respectfully traverse and submit that claims 1-3, and 5 have been shown to have "a specific, substantial, and credible utility", as detailed in the section above. Applicants therefore

request that the rejection of claims 1-3, and 5 under 35 U.S.C. § 112, first paragraph, be withdrawn.

## VI. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Landsman have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

This response is timely filed and Applicants believe no fees are due in connection with this response. However, should this be incorrect the Commissioner is authorized to charge any required fees or credit any overpayment to Deposit Account No. 50-0892.

Respectfully submitted,

October 16, 2003
Date

Lance K. Ishimoto Reg. No. 41,866

LEXICON GENETICS INCORPORATED
(281) 863-3333

**Customer # 24231**

AC008687. Homo sapiens chro...[gi:15887249] Links

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AUTHORS DOE Joint Genome Institute and Stanford Human Genome Center.
TITLE Direct Submission
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 157633)
AUTHORS DOE Joint Genome Institute.
TITLE Direct Submission
JOURNAL Submitted (03-AUG-1999) Production Sequencing Facility, DOE Joint Genome Institute, 2800 Mitchell Drive, Walnut Creek, CA 94598, USA
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www-shgc.stanford.edu
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  JOURNAL   Unpublished
REFERENCE   2  (residues 1 to 456)
  AUTHORS   Bardien-Kruger,S., Wulff,H., Arieff,Z., Brink,P., Chandy,K.G. and
            Corfield,V.
  TITLE     Direct Submission
  JOURNAL   Submitted (23-OCT-2000) SANBI, University of Western Cape,
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 FASTA searches a protein or DNA sequence data bank
 version 3.3t05 March 30, 2000
Please cite:
 W.R. Pearson & D.J. Lipman PNAS (1988) 85:2444-2448

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